Extramural papers of the month

By Nancy Lamontagne

Read the current Superfund Research Program Research Brief. New issues are published on the first Wednesday of each month.

Contaminated diet contributes to phthalate and bispenol A exposure

An NIEHS-funded researcher and colleagues report that an intervention designed to minimize exposure to bisphenol A (BPA) and phthalates actually led to increases in phthalate concentrations. The study found that people may be exposed to BPA and phthalates in their diets, even when they eat organic food that is prepared, cooked, and stored in non-plastic containers.

The researchers conducted a randomized trial with 10 families. Half of the families receiving a catered diet of local, fresh organic food that was not prepared, cooked, or stored in plastic containers. The other families received written recommendations to reduce phthalate and BPA exposures.

The people who received the meal replacement showed an unexpected increase in urinary di(2-ethylhexyl) phthalate (DEHP) metabolite concentrations, rising from a median of 283.7 nanomoles per gram at baseline to 7,027.5 nanomoles per gram during the intervention ($P<0.0001$). The families who received the written material had no significant changes in phthalate concentrations during this time period. The investigators also saw a statistically significant increase in total BPA concentration between baseline and intervention periods for the families receiving meal replacements, but not in the other families. To identify the source of the exposure, they tested the food ingredients used in the meal replacements and found DEHP concentrations of 21,400 nanograms per gram in ground coriander and 673 nanograms per gram in milk.

The researchers conclude that without regulation to reduce phthalate and BPA concentrations in food production, it may be difficult to develop effective and feasible interventions for the general population.

Citation: Sathyanarayana S, Alcedo G, Saelens BE, Zhou C, Dills RL, Yu J, Lanphear B. *(http://www.ncbi.nlm.nih.gov/pubmed/23443238)* 2013. Unexpected results in a randomized dietary trial to reduce phthalate and bisphenol A exposures. J Expo Sci Environ Epidemiol; doi: 10.1038/jes.2013.9 [Online 27 February 2013].

PBDEs may increase risk for Parkinson's disease

Findings from an NIEHS-funded study point to polybrominated diphenyl ethers (PBDEs) as a possible risk factor for Parkinson's disease and other neurodegenerative diseases.

PBDEs are used as flame retardants and are chemically similar to PCBs, which studies have suggested can increase risk for Parkinson's disease. To see if PBDEs are also neurotoxic, the researchers evaluated the *in vivo* and *in vitro* effects of PBDE mixture DE-71. Previous research showed that vesicular monoamine transporter 2 (VMAT2) mediates dopamine neuron vulnerability and can be inhibited by PBDEs. Thus, they were particularly interested in studying how deficits in VMAT2 expression and function might influence the neurotoxicity of DE-71.

The investigators found that DE-71 caused cell death in a dopamine-secreting cell line and also lowered the number of dopamine-secreting neurons isolated from mice that expressed normal amounts of VMAT2, as well as from mice that expressed approximately 5 percent of normal VMAT2 levels. Mice exposed to DE-71 had significant deposits of PBDE congeners in their brains, reductions in locomotor activity, and less dopamine in the area of the brain associated with Parkinson's disease. These changes were worse in animals deficient in VMAT2. The researchers conclude that their findings warrant additional laboratory and epidemiological research on PBDEs as a potential risk factor for Parkinson's disease and other neurological disorders.

Citation: Bradner JM, Suragh TA, Wilson WW, Lazo CR, Stout KA, Kim HM, Wang MZ, Walker DI, Pennell KD, Richardson JR, Miller GW, Caudle WM. *(http://www.ncbi.nlm.nih.gov/pubmed/23287494)* 2013. Exposure to the polybrominated diphenyl ether mixture DE-71 damages the nigrostriatal dopamine system: Role of dopamine handling in neurotoxicity. Exp Neurol 241:138-147.

Father's obesity could have epigenetic effects

A study partially supported by NIEHS found that newborns with obese fathers had significantly less DNA methylation of the insulin-like growth factor 2 (IGF2) gene. Since reduced DNA methylation of this gene is associated with a higher risk of

developing certain cancers, the study findings suggest that a father's obesity could influence his child's future health.

The researchers looked for associations between preconceptional obesity and changes in IGF2 DNA methylation. They examined DNA from 79 newborns whose mothers participated in the Newborn Epigenetics Study during pregnancy and also gathered information about both parents using questionnaires and medical records.

Even after adjusting for several maternal and newborn characteristics, they observed a persistent inverse association between DNA methylation in the offspring and paternal obesity (beta-coefficient was -5.28, P = 0.003). The researchers say that the changes in DNA methylation could result from obesity-related factors, such as diet or having diabetes, that were not measured in the study.

Citation: Soubry A, Schildkraut JM, Murtha A, Wang F, Huang Z, Bernal A, Kurtzberg J, Jirtle RL, Murphy SK, Hoyo C. *(http://www.ncbi.nlm.nih.gov/pubmed/23388414)* 2013. Paternal obesity is associated with IGF2 hypomethylation in newborns: results from a Newborn Epigenetics Study (NEST) cohort. BMC Med 11:29. [commentary]. *(http://www.biomedcentral.com/1741-7015/11/30/abstract)*

SOD1 can repress respiration

An NIEHS-supported study reports that an enzyme important in protecting cells from free radicals also helps repress respiration in rapidly dividing cells. The results reveal how yeast and cancer cells may repress respiration in favor of aerobic glycolysis, or fermentation, to promote rapid growth.

The researchers studied Cu/Zn superoxide dismutase (SOD1), which is known to help protect cells against oxidative stress. Using the yeast *Saccharomyces cerevisiae*, they revealed a new function for SOD1 in repressing respiration. When glucose and reactive oxygen are present, the enzyme binds to the casein kinase 1-gamma homologs Yck1p and Yck2p, protecting them from degradation. Yck1p and Yck2p are essential for respiratory repression, as well as nutrient sensing. Together, oxygen, glucose, and reactive oxygen make up a single circuit that can repress respiration through SOD1/casein kinase signaling. These results suggest that SOD1 acts as a metabolic focal point for integrating oxygen, nutrients (glucose), and reactive oxygen to direct energy metabolism.

Citation: Reddi AR, Culotta VC. *(http://www.ncbi.nlm.nih.gov/pubmed/23332757)* 2013. SOD1 integrates signals from oxygen and glucose to repress respiration. Cell 152(1-2):224-235.

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